Tubular Processing of the Glomerular Filtrate

As the glomerular filtrate enters the renal tubule (now called the tubular fluid), it flows through the proximal tubule, the loop of Henle, the distal tubule, the collecting tubule and finally the collecting duct.

As this tubular fluid passes down the tubules, its volume is reduced and its composition altered by the processes of tubular reabsorption and secretion, to form the urine that enters the renal pelvis. A comparison of the composition of the plasma and an average urine specimen illustrates the magnitude of some of these changes in the following table.

Substance	**Concentration in**		**U/P Ratio**
Glucose (mg/dL)	0	100	0
Na^+ (mEq/L)	90	150	0.6
Urea (mg/dL)	900	15	60
Creatinine	150	1	150

The rate at which different substances are excreted in urine represents the sum of the three processes: glomerular filtration, tubular reabsorption and tubular secretion.

Urinary excretion rate = Filtration rate - reabsorption rate + secretion rate.

Tubular Reabsorption

It involves:

1) Transport of the substance across the tubular epithelium into the renal interstitial fluid.

2) Transported from the interstitial fluid into the peritubular capillaries.

Tubular Secretion: Transport of substance from the blood in

peritubular capillaries into the renal tubule.

Types of transport across the tubular epithelium

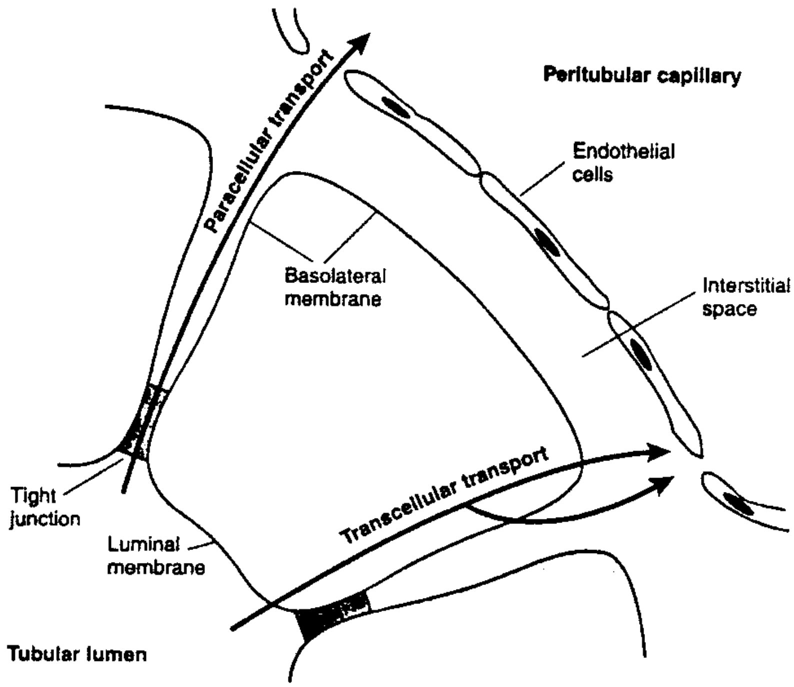

Fig. (4-1)

1. Transcellular: Solutes are reabsorbed or secreted through cells.
2. Paracellular: solutes are reabsorbed or secreted through the tight junctions between the cells.

Mechanism of tubular transport:

There are three basic principles by which solutes and water are transported across the tubular membrane:

A. Active transport:

1. Primary active transport.
2. Secondary active transport.
    a) Co-transport.

b) Countertransport.

B. Passive transport.

C. Pinocytosis.

A. Active transport:

It's against concentration or electrical gradient.

1- Primary active transport:

- The energy for the primary active transport comes from hydrolysis of ATP by membrane bound ATPase.
- The ATPase is a component of a carrier (transporter) that binds and moves solutes across the cell membrane.
- Sodium reabsorption across the proximal tubular epithelium is an example of the primary active transport.
- <u>At the basolateral border of the tubular epithelium;</u>

  Na^+ - K^+ ATPase pump extrudes 3 Na^+ into the interstitium in exchange for 2 K^+ that are pumped into the cell. This ion pump results in:-

- Creating a negative potential of about - 70 mV within the cell.
- Low intracellular Na^+ concentration.

- <u>At the luminal border:</u>

  Na^+ diffuses across the luminal membrane from the tubular lumen into the cell due the electrical and chemical gradient. (Fig. 4-2)

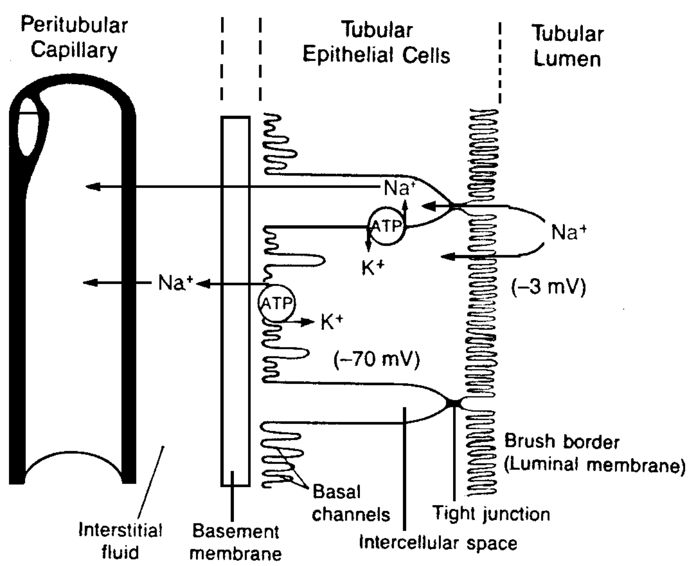

Fig. (4-2)

2. *Secondary active transport:*

This type of transport does not require energy directly from ATP or from the high-energy phosphate sources. It is of two types:

a) Co-transport: The reabsorption of one substance is linked to passive reabsorption of another substance. The direct source of energy is that liberated by simultaneous diffusion of another transported substance down its electrochemical gradient. The two substances bind to a specific carrier molecule and are co-transported together across the membrane. One of the substances diffuses down its electrochemical gradient while the second substance is transported against its chemical gradient e.g. secondary active transport of glucose. (Fig. 3-3)

At the luminal border:

- Glucose and Na^+ bind to a common carrier SGLT-2 in the luminal membrane. As Na^+ diffuses along its electrochemical gradient glucose is introduced into the cell.

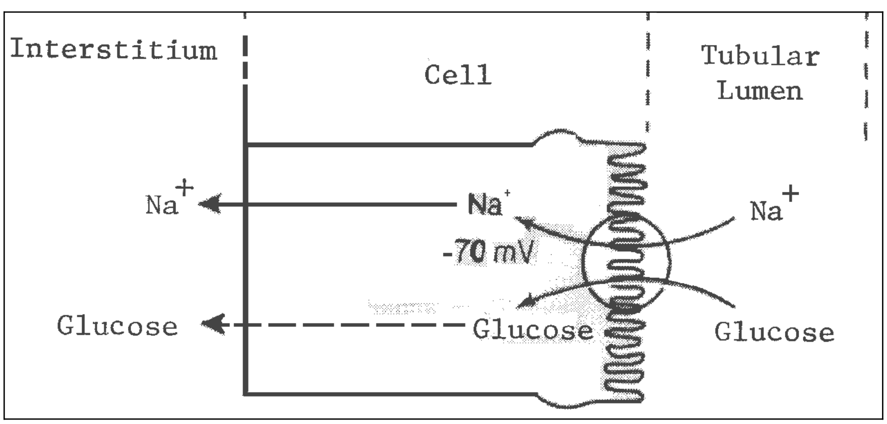

Fig. (4-3)

At the basolateral border:

- The Na^+ is pumped out of the cell into the lateral intercellular spaces.

- Glucose is transported by another carrier GLUT-2 into the interstitial

fluid by facilitated diffusion.

b) Countertransport:

The reabsorption of one substance is linked to secretion of another substance e.g. secondary active secretion of H^+ into the tubule. (Fig. 3-4)

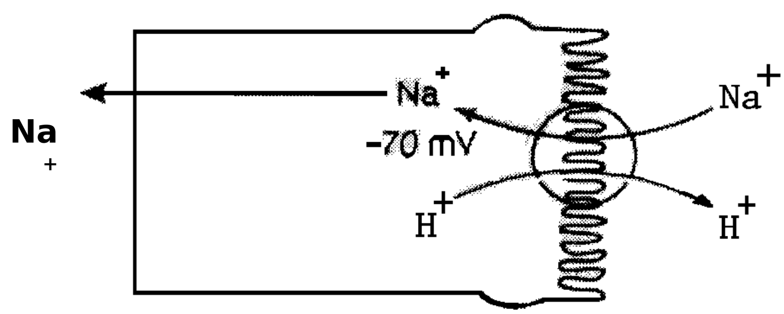

Fig. (4-4)

As Na^+ is carried to the interior of the cell, hydrogen ions are forced outward in the opposite direction into the tubular lumen by sodium - hydrogen counter transport protein in the brush border of the luminal membrane, of the proximal convoluted tubule.

B. Passive Reabsorption:

1. Passive Reabsorption of Chloride:

It occurs through paracellular pathway following Na^+ reabsorption.

The transport of positively charged Na^+ out of the lumen leaves the inside of the lumen negatively charged. This causes chloride ions to diffuse passively.

2. Osmosis of Water:

When solutes are reabsorbed out of the tubule, their concentration decreases inside the tubule while increasing in the interstitium.

This creates a concentration gradient that causes osmosis of water from the tubular lumen into the renal interstitium mainly through paracellular route.

3. Passive Reabsorption of Urea:

As water is reabsorbed from the tubule, urea concentration in the tubular lumen increases. This creates a concentration gradient favouring reabsorption of urea. About 50% of the filtered urea is passively reabsorbed from the tubule and the remainder passes into urine.

C. Pinocytosis:

It is an active transport mechanism for reabsorption of proteins and peptides in the proximal convoluted tubule. Proteins in the tubular fluid attach to the luminal membrane of the epithelial cells. This portion of the membrane then invaginates to the interior of the cell until it's completely pinched off. A vesicle is formed containing the protein, which is digested into amino acids.

These amino acids are reabsorbed through the basolateral membrane into the interstitial fluid.

■ Tubular Transport Maximum

- For many actively transported substance, there is a maximum rate at which each can be transported. The maximum rate that can be achieved is termed the transport maximum (Tm) for the substance expressed as mg/minute.
- Substances that are actively reabsorbed or secreted require a specific transport systems i.e. specific carriers and enzymes in the tubular epithelial cells. Therefore, the reason that actively transported solutes exhibit a transport maximum is that the carrier system becomes saturated as the tubular load increases.

Solutes that exhibit T_m-limited reabsorption:

- Glucose, amino acids, phosphates and sulphates .
- The affinity of the transport system for many substances with Tm-Limited reabsorption is so high that the entire filtered load is reabsorbed from the tubular fluid so long as the transport system is unsaturated. For example, reabsorption of glucose and amino acids is completed if the filtered load does not saturate the transport system.

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- **Threshold for substances that have a tubular maximum:**

  Substances that have a reabsorptive maximum have a threshold concentration in the plasma below which none of the substance appears in the urine and above which progressively large quantities appear.

Gradient - time Transport

All substances that are reabsorbed by diffusion do not exhibit a transport maximum. Instead, transport of this type is termed gradient-time transport as it is determined by:

1. The Electro-chemical gradient' for the substance across the membrane.
2. The time that the fluid containing the substance remains within the tubule which in turn depends on the tubular flow rate.

Some actively transported substances also obey the gradient-time transport, e.g. Na^+ reabsorption by the proximal tubules, as it is determined by:

1-The concentration of Na^+ in the proximal tubule: the greater the concentration of Na^+ in the proximal tubule, the greater the reabsorption rate.

2-The rate of flow: The slower the flow rate of the tubular fluid, the greater the percentage of Na^+ that can be reabsorbed from the proximal tubule.

Absorption by the peritubular capillaries

Fluid and electrolytes are reabsorbed from the renal interstitium into the peritubular capillaries by bulk flow as the peritubular capillaries behave like venous end of capillary.

- **The forces that act across the peritubular capillaries are:**

1-Forces that favour reabsorption:

a) The colloidal osmotic pressure of the peritubular capillaries (about 32 mmHg).

b)The hydrostatic pressure in the renal interstitium (about 6mmHg).

2- Forces that oppose reabsorption:

a) The hydrostatic pressure inside the peritubular capillaries (about 13mm Hg).

b)The colloidal osmotic pressure of proteins in the renal interstitium (about 15mm Hg).

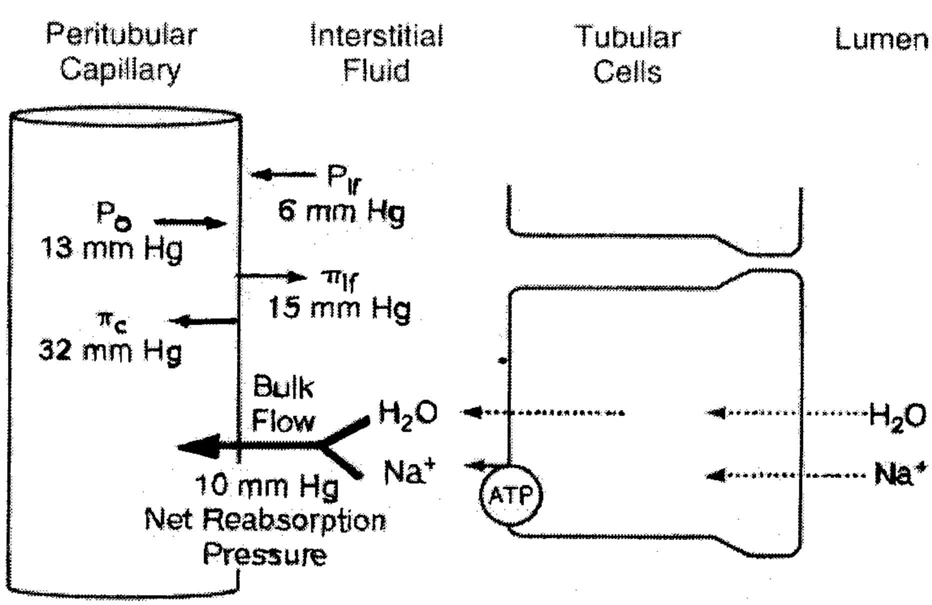

Fig. (4-5): shows these forces acting across the peritubular capillaries.

Net reabsorptive Force = (32 + 6) - (13 + 15)

= 38-28= 10 mmHg

Through changes in the hydrostatic and colloidal osmotic pressure of the renal interstitum and of the peritubular capillaries, the uptake of fluid and solutes by the peritubular capillaries is matched to the net reabsorption of water and solutes from the tubular lumen into the interstitium.

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